The Egyptian Journal of Hospital Medicine (2009) Vol., 34: 143–154

Effect Of Nalbuphine (A Narcotic Drug)On Some Hematological And Biochemical Parameters Of Male Albino Rat

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Abstract

Among narcotic drugs of major importance in medicine, is nalbuphine hydrochloride. It is a potent analgesic, has been effectively used in the treatment of moderate to severe pain, in post-operative analgesia, for labor analgesia and as a component of balanced anesthesia. Commercially, nalbuphine hydrochloride is known as nubain or nalufin.

The present study aimed to investigate the possible noxious impacts of this drug on some hematological and biochemical parameters of male albino rat (***Rattus norvegicus***). So, Sixty adult rats weighing 140-150 gm . were used to study erythrocytes (R.B.Cs) & leucocytes (W.B.Cs) counts , hemoglobin (Hb) concentration , hematocrit (Hct) value, mean corpuscular volume (MCV) , mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC). Besides, studying the biochemical analysis of kidney function including urea and creatinine concentrations, in addition to thyroid hormones , triiodothyronine (T3) and thyroxine (T4) levels.

The experimental groups were injected twice time daily intramuscularly with the drug at the dose levels of 0.2 and 0.4 mg/100gm. b.wt. for 15 and 30 days.

Nalbuphine hydrochloride treated rats displayed deleterious alterations in their hematological and biochemical analysis .

The data of hematological investigations revealed a marked decrease in RBCs , Hb , Hct and MCV in groups treated with low or high dose of nalbuphine for 30 days. Also, a significant decreases were detected in R.B.Cs , Hb and MCH in rats treated with high dose of nalbuphine for 15 days. While, Hb concentration , Hct value, MCV and MCH showed insignificant changes in rats treated for 15 days with the low dose. On the other hand, MCHC and W.B.Cs showed insignificant changes throughout all treated groups.

Biochemical studies on the serum indicated a marked increase in urea and creatinine in all groups treated with nalbuphine. On the other hand ,T3 and T4 exhibited a significant decrease after treatment with nalbuphine.

In conclusion, these deleterious changes give an alarm to be aware in using such drugs from the narcotic group.

Key Words: Nalbuphine hydrochloride , Hematological and Biochemical Parameters , Narcotic , Albino rat , Serum .

Introduction

Relief of pain is one of the greatest objectives in medicine. As pain is a very common symptom of disease and trauma , drugs with a pain relieving action are called analgesics , and are commonly classified as narcotic and non – narcotic.

Strong analgesics that act on pain perception within the central nervous system are classified under the term opiates or opioids, they are used interchangeably with the term narcotic analgesics . Weaker analgesics, which called non-narcotics, act chiefly by a peripheral mechanism and are used for musculo-skeletal pain. In addition to their relieving action, many of them are also lowered the body temperature (antipyretic) and possess anti-inflammatory activity (Bowman and Rand, 1980 and Crossland, 1980).

Among narcotic drugs of major importance in medicine, is nalbuphine hydrochloride. It is a potent analgesic which possesses both narcotic – like agonist and antagonist properties. It is an

interesting synthetic analgesic drug with some apparent potential advantages over analgesic such as morphine and pentazocine (Kay and Cohen,1983).

Nalbuphine has been effectively used in the treatment of both moderate to severe acute pain, i.e. for the relief of pain in patients with trauma , renal and biliary colic and in those patients suffering from acute myocardial infarction (Lewis,1980). Also , nalbuphine hydrochloride is used for the relief of moderate to severe chronic pain, i.e. pain due to advanced malignancy (Stambaugh,1982).

In addition ,nalbuphine has been also investigated as a component of balanced anaesthesia (Kovacs *et al.*,1993). Nalbuphine is used also in post-operative analgesia for relieving pain, i.e after total hip replacement (Foumier *et al.*,2000).

In 2004 , Mark *et al.* declared that nalbuphine is used in treated vasoocclusive sickle cell pain in children and as labor analgesia.

Non-medical abuse of prescription narcotics is not a new phenomenon , but such abuse has been increasing in recent years. Also , medication abuse may occur under a variety of circumstances, such as by healthcare professionals who have direct access to the medication by individuals for whom the medication has been prescribed but who use it recreationally for other than its intended therapeutic purpose . Additionally, individuals other than whom the medication has been prescribed may misuse it (Paul and Rolly, 2006) .

In recent years, narcotics abuse and the crime that gose along with it have begun to present a serious threat to the future and national security. The rapid increase in the use of narcotic not required for medical needs, especially by-children, adolescents and young people – has a direct and very destructive impacts on the physical and mental health of the nation. It is thus clear that the illegal abuse of these drugs has created tremendous health, social and economic problems, particularly in developing countries. Moreover, tremendous numbers of people have been estimated to be killed by such illegal abuses of these drugs.

For example , according to the 2003 National Survey of Drug Use and Health of the United States, there were 6.3 million current users and 31.2 million .lifetime individuals aged 12 or older who misused pain relievers , tranquilizers , stimulants, and sedatives (Substance Abuse and Mental Health Services Administration, 2004 and Edward, 2006).

Also, the increase in the number of persons addicted to narcotics became a steady trend at the end of the 1980s, starting in the mid-1990s in Russia, the process of the spread of narcotic ailments became noticeably more rapid, according to the data of the Russian Federation Ministry of Health. The number of adolescents who suffer from narcotics abuse has increased by 14.8 times in the past ten years (Shcherbakova , 2005).

Beginning in the early 1990s , drug abuse spread quickly in China . The number of registered drug addicts increased from 70,000 in 1990 to 1 million by the end of 2002 . (Chengzheng *et al* ., 2004).

Regarding the situation in Egypt , there are no concrete records of addicts or fatalities caused by abuses of such drugs, therefore , studies were done in this field to enlighten the adverse effects of the use of such drugs in the animal body , to face and confront this situation which is severely endangering the welfare of the whole country.

Material And Methods

Sixty mature male albino rats ***(Rattus norvegicus)*** ranging in weight from 140-150gm., were essentially obtained from *Schistosama* Biological Supply Program (SBSP). Theodor Bilharz Research Institute. The rats were randomly allocated at into two groups : **The first group** (20 rats) were kept as control being observed under the same laboratory conditions and were injected daily intramuscularly with saline solution (0.9% NaCl). **The second group** (40 rats) were in turn - allocated into two equal subgroups (i.e.20 rats each). These rats were intramuscularly injected with the drug- twice time in a daily manner (at 8 am and 8 pm) –as follows:

- **The first subgroup** was given 0.2mg/100gm . body weight.
- **The second . subgroup** was given 0.4mg/100gm . body weight.

These drug doses were left to act for 15 and 30 days. All animals were kept under suitable care before the experiment in clean laboratory conditions, fed on standard diet of compact chops , in addition of milk and water *ad-libitum*. At the end of experimental periods, animals were sacrificed. Blood samples were collected on heparinized capillary tubes for the hematocrit value which was determined according to the method of Rodak (1995). Another part of blood was collected on EDTA for the hematological examination . Red and white blood cells counts were performed using improved hemocytometer according to Dacie and Lewis (1991). Hemoglobin concentration was estimated according to Dacie and Lewis (1991). MCV , MCH and MCHC were calculated according to Dacie and Lewis (1993). For Biochemical analysis, blood samples were collected in clean dry centrifuge tubes for serum preparation. Blood samples were allowed to clot for one hour then centrifuged at 3500 r.p.m for 15 minutes. Clear non haemolysed serum was separated and kept in a deep freeze at-20°C until assayed . Serum content of urea and creatinine were estimated according to the methods described by Patton & Crouch (1977) and Bartels & Bohmer (1972), respectively . Determination of thyroxine (T4) was carried out by using solid phase enzyme – immunoassay. Measurement of serum tri - iodothyronine (T3) concentration was done by using enzyme-immunoassay kit purchased from (Boehringer Manheim West Germany). The methods were carried out according to Wood (1980) .

Data analysis:

The obtained results were statistically analyzed by using the student "t"-test according to the method of Snedecor and Cochran.(1980).

Results

The data represented in table (1) displayed the effect of nalbuphine on ery - throcytes (R.B.Cs) counts of male albino rats. The findings indicated that treated rats showed highly significant decrease ($P < 0.01$) after 30days, but this decrease was less pronounced ($P < 0.05$) after 15 days with both low and high doses.

Table(2) also illustrate the effect of nalbuphine on hemoglobin (Hb) content of rats. Nalbuphine was found to induce a significant diminutions ($P < 0.05$) of Hb concentrations in rat groups treated with high dose and the group treated with low dose for 30 days. But, no marked change was detected in Hb content of rats treated with low dose for 15 days as compared to the corresponding mean control values.

The hematocrit (Hct) value (Table 3) also showed a response to the effect of nalbuphine under investigation. The results recorded a significant decrease ($P<0.05$) of mean Hct value in rat groups treated with low and high doses for 30days, but no alterations were recorded in that groups after 15 days.

Table (4) demonstrate the effect of nalbuphine on the values of the mean corpuscular volume (MCV) of male albino rats. Although there was a noticeable decrease ($P<0.05$) and ($P < 0.01$) in MCV of groups treated with low and high dose, respectively for 30 days, the other groups treated for 15 days showed insignificant changes.

Table (5) display the effect of nalbuphine on mean corpuscular hemoglobin (MCH) of albino rats. Only, groups treated with high dose recorded a significant decrease ($P<0.05$) , where the other group that treated with the low dose of nalbuphine appeared no significant change.

The data represented in table (6) displayed the effect of nalbuphine on the mean corpuscular hemoglobin concentration (MCHC) of male albino rats. Nevertheless, there was difference in MCHC between the treated groups and the corresponding control , but this change was statistically insignificant.

Generally, table (7) illustrate that the leucocytes (W.B.Cs) counts were not affected by nalbuphine throughout the experiment.

The results represented in table (8) revealed that there was a high significant increase ($P < 0.01$) in the urea level in rat groups treated with low and high doses of nalbuphine for 15days. It significantly

increased (P<0.05) after 30 days in rats treated with high dose only.

Table (9) also, illustrate the effect of nalbuphine on serum creatinine concentration of male albino rats. It is worthy to point out in this respect that the highest elevation (P < 0.01) was observed in all groups treated with high doses after the two periods, and groups treated with the low dose after 30days which, it exhibited a significant increase (P < 0.05) in rats treated with the low dose for 15days.

Regarding to the table (10) , the triiodothyronine hormone (T3) levels also showed some response to the nalbuphine under investigation . The results showed a marked decrease (P < 0.05) in T3 levels of all treated groups.

In table (11) the data showed a significant decrease (P < 0.05) of thyroxine hormone (T4) in all groups treated with high dose of nalbuphine for 15and 30 days. Also, it exhibited a significant decrease (P < 0.05) in rats treated with the low dose for 30 days.

Table(1): Effect of nalbuphine on erythrocytes (RBCs) count ($x10^6/mm^3$) of male albino rats.

Groups / Duration of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean±S.E.	Mean±S.E.	%of change	P value	Mean ±S.E.	%of change	P value
15days	8.4 ± 0.07	8.1 ± 0.06	-3.57	P<0.05*	7.9 ± 0.08	-5.95	P<0.05*
30days	8.6± 0.08	7.3± 0.15	-15.12	P<0.01**	7.4 ± 0.13	-13.95	P<0.01**

All values were expressed as mean ± standard error.
*(Significant).
**(Highly Significant).

Table(2): Effect of nalbuphine on hemoglobin (Hb) content (g/dl) of male albino rats.

Groups / Duration of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean ± S.E.	%of change	P value	Mean ±S.E.	%of change	P value
15days	14.55± 0.26	14.01± 0. 18	-3.71	ins.	13.09± 0.42	-10.03	P<0.05*
30days	14.63± 0.26	13.17± 0.51	-15.45	P<0.05*	12.14± 0.46	-17.02	P<0.05*

All values were expressed as mean ± standard error.
Ins.(insignificant).
*(Significant).

Table(3): Effect of nalbuphine on hematocrit (Hct) value (%) of male albino rats.

Groups / Duration of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean ±S.E.	% of change	P value	Mean ± S.E.	% of change	P value
15days	38.31±2.67	33.34± 1.38	-12.97	ins.	33.16± 1.67	-13.44	ins.
30days	37.90± 2.46	31.26±1.29	-17.52	P<0.05*	31.48± 1.60	-16.92	P<0.05*

All values were expressed as mean ± standard error.
Ins.(insignificant).
*(Significant).

Table(4): Effect of nalbuphine on the mean corpuscular volume (MCV) (fl) of male albino rats.

Groups / Duration of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean ±S.E.	% of change	P value	Mean ± S.E.	% of change	P value
15days	45.61±2.6	41.16± 1.32	-9.76	ins.	41.97± 1.59	-7.98	ins.
30days	44.07± 0.29	42.82±0.34	-2.84	P<0.05*	42.54± 0.21	-3.47	P<0.01**

All values were expressed as mean ± standard error.
Ins.(insignificant).
*(Significant).
**(Highly Significant).

Table(5): Effect of nalbuphine on the mean corpuscular hemoglobin (MCH) content (pg) of male albino rats.

Groups / Duration Of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean ± S.E.	% of change	P value	Mean ± S.E.	% of change	P value
15 days	17.32± 0.20	17.30 ± 0.31	- 0.12	ins.	16.57± 0.10	- 4.33	P<0.05*
30 days	17.01± 0.18	16.95± 0.17	- 0.35	ins.	16.41 ± 0.15	- 3.53	P<0.05*

All values were expressed as mean ± standard error.
Ins.(insignificant).
*(Significant).

Table(6): Effect of nalbuphine on the mean corpuscular hemoglobin concentration (MCHC) (%) of male albino rats.

Groups / Duration Of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean ± S.E.	% of change	P value	Mean ± S.E.	% of change	P value
15 days	37.98± 1.42	42.02 ± 1.46	+10.64	ins.	39.47± 1.44	+ 3.92	ins.
30 days	38.60± 1.38	39.57± 1.40	+2.51	ins.	38.56 ± 1.41	- 0.10	ins.

All values were expressed as mean ± standard error.
Ins.(Insignificant).

Table(7): Effect of nalbuphine on Leucocytes (WBCs) count ($x10^3/mm^3$) of male albino rats.

Groups / Duration Of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean ± S.E.	% of change	P value	Mean ± S.E.	% of change	P value
15 days	5.613± 0.37	6.031 ± 0.36	+7.45	ins.	5.273± 0.22	-6.06	ins.
30 days	5.880± 0.35	6.465± 0.31	+9.95	ins.	6.513 ± 0.39	+10.77	ins.

All values were expressed as mean ± standard error.
Ins.(Insignificant).

Table(8): Effect of nalbuphine on urea concentration (mg/L) of male albino rats.

Groups / Duration of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean ±S.E.	%of change	P value	Mean ± S.E.	%of change	P value
15days	26.74± 0.33	43.53±1.04	+62.79	$P<0.01^{**}$	44.60 ± 1.75	+66.79	$P<0.01^{**}$
30days	27.56± 0.34	32.86±2.43	+19.23	$P<0.05^{*}$	35.19± 2.16	+27.69	$P<0.05^{*}$

All values were expressed as mean ± standard error.
*(Significant).
**(Highly Significant).

Table(9): Effect of nalbuphine on creatinine concentration (mg/l) of male albino rats.

Groups / Duration of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean ±S.E.	%of change	P value	Mean ± S.E.	%of change	P value
15days	14.48± 0.23	21.11±1.92	+45.79	P<0.05*	24.04± 1.70	+66.02	P<0.01**
30days	13.78± 0.39	26.01± 1.41	+88.75	P<0.01**	27.96± 1.85	+102.90	P<0.01**

All values were expressed as mean ± standard error.
*(Significant).
**(Highly Significant).

Table(10): Effect of nalbuphine on triiodothyronine (T3) level (ng/ml) of male albino rats.

Groups / Duration of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean±S.E.	% of change	P value	Mean ± S.E.	%of change	P value
15days	1.38± 0.07	1.11±0.08	-19.56	P<0.05*	1.12 ±0.09	-18.84	P<0.05*
30days	1.36±0.07	1.09±0.07	-19.85	P<0.05*	1.13±0.06	-16.91	P<0.05*

All values were expressed as mean ± standard error.
*(Significant).

Table(11): Effect of nalbuphine on Thyroxine (T4) level (µg /dl) of male albino rats.

Groups / Duration of experiment	Control Groups	Treated Groups					
		Low Dose Groups			High Dose Groups		
	Mean ± S.E.	Mean±S.E.	% of change	P value	Mean ± S.E.	% of change	P value
15days	11.60± 1.04	9.57±0.96	-17.5	ins.	8.02± 1.01	-30.86	P<0.05*
30days	11.91±1.09	8.10± 1.15	-31.99	P<0.05*	7.94± 1.07	-33.33	P<0.05*

All values were expressed as mean ± standard error.
Ins.(Insignificant).
*(Significant).

Discussion

Drugs – in general – and narcotics – in particular – have , beside their advantages , some hazardous effects on the body organs . It should be recalled that most of the work carried out on the narcotics have been emphasizing mainly on their medical application together with limited physidogical and biochemical aspects. Very little attention has been paid to investigate the possible impacts of such drugs – in general - and nalabupline – in particular – on the hematological and biochemical parameters of the body organs. That is why – as previously mentioned – the present work was carried out , aiming at filling some of these gaps by investigating the impact of nalbuphine as an interesting analgesic with apparent potential

advantages over other analgesics on such vital and fertile fields.

Nalbuphine hydrochloride , from the pharmacokinetic point of view is well established among the narcotic drugs as one of the first synthetic opioids that offered distinct advantages to be highly potent analgesic over morphine , has been effectively used in treatment of moderate to severe pain , in pre and post – operative analgesia , for labor analgesia and as a component of balanced anaesthesia (Kovacs *et al.,* 1993 ; Foumier *et al.,* 2000 and Mark *et al.,* 2004).

Therefore , the present study was done to illustrate and emphasize the possible noxious adverse effects of nalbuphine hydrochloride on some hematological and biochemical parameters of albino rat ***(Rattus norvegicus)*** as one of the mammalian representative animal.

In the present investigation , it was observed that the application of nalbuphine hydrochloride in both doses ***(low and high doses)*** and for two different periods (***15 and 30 days***) in the male albino rats had caused certain alterations. These changes were found to be dose and time dependent.

Hematological parameters are a valuable tool for assessing the injures that caused by certain drugs. The RBC count is most useful as raw data for calculation of the erythrocyte indices MCV and MCH. Decreased RBC is usually seen in anemia of any cause. Results of the present investigation revealed that erythrocytes (R.B.Cs) count , hemoglobin (Hb) content and hematocrit (Hct) values were almost highly significant deceased throughout the experimental periods in groups treated with low and high doses of nalbuphine. These changes induced by nalbuphine may be due to the prevention of red blood cell synthesis via inhibition of erythropoiesis in the bone marrow. Also, our results revealed a significant diminished of MCV and MCH specially , after treatment with the high dose of nalbuphine for long periods. These results reflect that nalbuphine administration led to a microcytic hypochromic anaemias. Similar to these findings , some investigators observed hematological changes in animals treated with different narcotics . They reported that the reduction in these parameters may be attributed to internal hemorrhage microcytic or hypochromic anemia possibly as a consequence of the effect of these drugs on bone marrow , spleen and liver (Moran *et al.,* 1995 ; El-Shennawy ,1999 ; El-Sherif *et al.,* 2002 and Gaskill *et al.,* 2005). Our results were also in accordance with some histological changes induced by nalbuphine in the form of early inflammatory reactions in the liver tissues with dialation and damage of the blood vessels and hemorrhage inside the blood vessels (Rosow *et al.,* 1982 ; Ashry *et al.,* 1990 ;Kamel , 2000 and Abo Elwafa , 2007). The decrease of Hb level accompanied with decrease in erythrocytes from circulation may be due to as a result of extravassation of blood . Also , the reduction in Hct value observed in the present work may probably due to haemolysis of red blood cells.

The total leucocytic count in the present study remained unchanged in all experimental groups . This observation conform with those presented by Atalan *et al.* (2002). Generally , the discrepancies observed between the various research studies may be attributed to dose variations as well as the duration of drug intake.

The present results clearly indicated that nalbuphine in both doses significantly and highly significantly elevated serum urea and creatinine. In view of these data, it could be assumed that nalbuphine hydrochloride administration to rats causes a kidney dysfunction which may lead to highly significant increase in both urea and creatinine. Therefore, the marked elevation of urea and creatinine levels in rat serum might reflect the damage of kidney tissue. These results conform with those by Atici *et al.* (2005) , they recorded that metabolites of the drugs that are excreted from the kidneys may cause cellular damage leading to kidney dysfunction. In this respect our results were in agreement with those recorded by Jaquenod *et al.* (1998); Chery (2005); Gupta *et al.* (2008) and Habibey & Toroudi (2008) . They demonstrated a significant increase in serum urea and creatinine in rats treated with different drugs related to opioid group.

In the present study the results obtained for T3 (tri – iodothyronine) and T4 (Thyroxine) levels revealed a remarkable

depletion in rats treated with low and high doses of nalbuphine hydrochloride. The depletion of T4 level induced by the low dose was appeared after 30 days of treatment . Many authors reported significant decrease in T3 and T4 after treatment with these types of drugs . Bhargava *et al.* (1988) reported that administration of methimazole decreased the serum concentration of T3 and T4. In 1989 , Anandalaxmi and Vijayan showed that naloxone drug could cause changes in thyroid function in male rats . Also, Balon *et al.* 1991 reported that treatment with diazepam led to decrease in T4 in panic disorder patients. In this respect our results were in agreement with those recorded by Miyawaki *et al.* (2003); Cansu *et al.* (2006) ; Mitchell *et al.* (2006) and Verrotti *et al.* (2008

Finally , this may interpret the noxious impacts of such drug on the albino rat. However , it is worthy to mention that this point of research is still in need for more investigations , to throw the light and explain these impacts consequences of nalbuphine drug.

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تأثير النالبوفين (عقار مخدر) على بعض القياسات الدموية والكيموحيوية فى ذكور الجرذان البيضاء

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من المعروف أن العقاقير المصنعة ، قد أنتجت بصورة أساسية للاستخدامات الطبية التى تستهدف معالجة الإنسان من الأمراض المختلفة للإبقاء على حياته سليما ، ومن بين هذه العقاقير مواد تستخدم كمهدئات ومسكنات للآلام المختلفة ، وأيضا كمخدر عام قبل العمليات الجراحية0

يعتبر عقار النالبوفين هيدروكلوريد من هذه العقاقير المخدرة المخلقة والتى تستخدم فى تخفيف الآلام ولها أهمية كبيرة فى مجال الطب0 وهو يعتبر مخدر قوى ، ويستخدم بكفاءة فى علاج الآلام المتوسطة والحادة 0 وقد أثبت النالبوفين هيدروكلوريد بصفه عامة كفاءته العالية كالمورفين فى القضاء على الآلام الظاهرة بعد العمليات الجراحية أو كمسكن قوى لآلام الأورام أو فى تقنيات التخدير0

والاستخدام الغير طبى للمواد المخدرة والمسكنات عموما ليس ظاهرة جديدة ولكنه فى زيادة مستمرة وخاصة فى السنوات الأخيرة 0 ويؤدى سوء الاستخدام المفرط للمسكنات خارج المجال الطبى وخاصة بواسطة الأطفال والمراهقين والشباب إلى تأثيرات مباشرة ومدمرة على النواحى الجسدية والعقلية للإنسان مما يمثل تهديدا خطيرا للمستقبل والأمن القومى ويترتب عليها جرائم وخيمة 0

ولذلك جاءت هذه الدراسة لتبحث أثر مثل هذه الأضرار الجانبية المحتملة لهذه العقاقير وخاصة عقار النالبوفين هيدروكلوريد والمعروف تجاريا باسم (النيوبين أو النالوفين) على بعض القياسات الدموية والكيموحيوية فى الجرذان البيضاء كمثال للحيوانات الثديية0

وقد تم تحديد الجرعات فى هذه الدراسة بناء على مقدار الجرعة المساوية للجرعة العلاجية للإنسان المستخدمة لتسكين الآلام0 وقد قدرت بـ 0.2 ملليجرام لكل 100جرام من وزن الجسم للجرذ بالإضافة إلى جرعة قدرها 0.4 ملليجرام لكل 100جرام من وزن جسم الجرذ كمؤشر لسوء الاستخدام0 واستخدم فى هذه الدراسة عدد 60 من ذكور الجرذان البالغة والتى يتراوح وزنها بين 140 – 150 جم وقسمت إلى مجموعتين:

– المجموعة الأولى مكونه من 20 جرذ واعتبرت كمجموعة ضابطة حيث تركت فى نفس الظروف المعملية وحقنت يوميا فى العضل بمحلول ملحى (0.9٪ كلوريد صوديوم) لمدة 15 و 30 يوما0

– المجموعة الثانية مكونه من 40 جرذ ، قسمت على التوالى لمجموعتين فرعيتين متساويتين (20 جرذ لكل مجموعة) ، وحقنت كلا من المجموعتين بالعقار فى العضل مرتين يوميا كالآتى:

- المجموعة الفرعية الأولى : حقنت بـ 0.2 ملليجرام/100جرام من وزن الجسم0
- المجموعة الفرعية الثانية : حقنت بـ 0.4 ملليجرام/100جرام من وزن الجسم0

وترك العقار ليتفاعل مع الجسم لفترات 15 يوم و 30 يوم فى كل من المجموعتين التجريبيتين 0 وأظهرت النتائج ما يلى:

1) لوحظ انخفاضا ملحوظا فى عدد خلايا الدم الحمراء وتركيز الهيموجلوبين إضافة إلى نسبة الهيماتوكريت فى المجموعات المعاملة بالجرعة المنخفضة والعالية من النالبوفين لمدة 30 يوم. كما لوحظ انخفاضا معنويا فى خلايا الدم الحمراء وتركيز

الهيموجلوبين وحجم كرات الدم الحمراء وكذلك الهيموجلوبين النسبى لعدد كرات الدم الحمراء فى المجموعة المعاملة بالجرعة العالية من النالبوفين لمدة 15 يوم.

بينما لم يتغير تركيز الهيموجلوبين ونسبة الهيماتوكريت فى الجرذان المعاملة بالجرعة المنخفضة لمدة 15 يوما0 وسجلت النتائج عدم تأثر عدد خلايا الدم البيضاء فى جميع مجموعات التجريب.

2) ازداد مستوى اليوريا والكرياتينين زيادة معنوية عالية خاصة فى الجرذان المعاملة بالجرعة العالية من النالبوفين.

3) أظهرت النتائج أيضا انخفاضا معنويا فى مستوى الثيروكسين وثلاثى يودالثيرونين فى جميع المجموعات المعاملة بالنالبوفين عدا الجرذان المعاملة بجرعة منخفضة من النالبوفين لمدة 15 يوم حيث ظل فيها مستوى الثيروكسين دون تغير.

ويتضح من النتائج السابقة أن عقار النالبوفين هيدروكلوريد كعقار مخدر له تأثيرات واضحة على فسيولوجيا الجسم خاصة عندما يستخدم بجرعات عالية ولفترات طويلة من الوقت ، مما يعكس أثرا بالغا على وظائف الجسم.